

REMARKS

Claims 1-33 are pending in the present application. In the Office Action dated July 11, 2007, the Examiner acknowledged the Applicant's election, with traverse, of the claims identified in Group I (claims 1-18), and the species compounds that bind to Topo II and inhibit its activity, compounds that bind to HSP90 and inhibit its activity, cancer treatment, and solid tumors. In response to the restriction requirement dated July 11, 2007, the Applicant hereby provisionally elects, with traverse, to continue prosecution of the claims identified in Group I (claims 1-18). Per the Examiner's instructions, the Applicant further elects, with traverse, as follows: the species of A-1 (Geldanamycin or a derivative or analogue thereof/17-Allylamino, 17- demethoxygeldanamycin (17AAG)), the species of B-1 (a Podophyllotoxin and derivatives or analogues thereof), the species of C-1 (etoposide (VP16)), and the species of E (solid tumors of the lung). The Applicant also reserves the right to later file one or more divisional applications directed to the subject matter of the non-elected claims.

The foregoing election notwithstanding, the Applicant respectfully traverses the restriction requirement, and respectfully requests reconsideration and withdrawal of the restriction requirement as set forth below.

In the Office Action, the Examiner alleges that there is no special technical feature linking the inventions of Groups 1-13, that defines a contribution over the prior art, as required by PCT Rule 13.2. However, to the contrary, the Applicant maintains that the unifying inventive feature is that agents that attenuate Topo II activity may be combined with a second agent that inhibits HSP90 and have improved synergistic

effects on cancer treatment not previously shown or taught by the prior art.

The prior art reference cited by the Examiner, Münster et al. (Clinical Cancer Res. 2001, 7:2228-2236, IDS) ("Münster"), does not show or teach the inventive unifying feature common to the inventions of Groups 1-13, that Topo II and HSP90 interact such that a combination of agents that specifically inhibit these individual protein has a synergistic effect. Although Münster discloses that ansamycin antibiotics such as 17-AAG (an HSP90 inhibitor) and doxorubicin may be combined, nowhere in Münster is the term "topoisomerase II" used or the effect of either of these agents on Topo II described. Even though doxorubicin has been shown to inhibit Topo II, which is critical to DNA function, its effect on Topo II is not disclosed nor discussed in Münster. Rather, Münster simply describes the effect of these agents on apoptosis (studied by looking at the nuclei) and does not show synergy in terms of cell death or proliferation. There is no suggestion that any of the effects are related to the interaction between HSP90 and Topo II.

Moreover, a skilled person may consider Münster to relate to the study of HSP90 modulated signaling pathways (i.e., RB pathways). It is well known that HSP90 inhibitors are effective in chemotherapy because they modulate signaling pathways. As such, a skilled person might conclude that doxorubicin may not be effective in chemotherapy because it is modulating Topo II (which is not a mediator of signal transduction). Accordingly, Münster does not show or teach the unifying feature of the present invention, namely, the modulation of Topo II.

Thus, the Applicant respectfully submits that the special technical feature of the inventions of Group 1-13 constitutes a special technical feature as defined by PCT Rule

13.2 as it defines a contribution over the prior art.

Lastly, in the Office Action, the Examiner stated that claims 1-18 of Group I as drawn to compounds that bind to Topo II and inhibit its activity, compounds that bind to HSP90 and inhibit its activity, cancer treatment, and solid tumors contain claims directed to patentably distinct species. The Examiner has issued a further restriction to specific molecules and specific types of solid tumors; however, the classes of compounds in each sub-group share similar characteristics and perform similar functions such that a search of compounds that bind to Topo II and inhibit its activity or compounds that bind to HSP90 and inhibit its activity would not impose an unreasonable burden on the Examiner. For example, geldanamycin and radicicol both share the same binding site (the N-terminal domain of HSP90) and similarly interfere with the function of HSP90. As such, the Examiner is not presented with an unreasonable burden in searching the prior art covering various embodiments of the Applicant's invention: (a) compounds that bind to and inhibit HSP90 and (b) compounds that bind to and inhibit Topo II for the purposes of (c) treating solid tumors.

For the foregoing reasons, the Applicant respectfully requests that the Examiner withdraw the restriction requirement.

A favorable action on the merits is respectfully requested.

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Conclusion

This response is being submitted with a two-month extension. In the case any fee is owed, please charge deposit account number 03-3975 (ref. 67074-312021). If, for any reason, the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (213) 488-7100 to discuss the steps necessary for placing the application in condition for allowance should the Examiner believe that such a telephone conference would advance prosecution of the application.

Respectfully submitted,

PILLSBURY WINTHROP SHAW PITTMAN LLP

Date: October 11, 2007

By: _____



Carolyn S. Lu
Registration No. 56,817
Attorney for Applicants

725 South Figueroa Street, Suite 2800
Los Angeles, CA 90017-5406
Telephone: (213) 488-7100
Facsimile: (213) 629-1033